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Chapter

Distraction Osteogenesis: Biological Principles and Its Application in Companion Animals

Guilherme Domingos, Henrique Armés, Isabel Dias, Carlos Viegas and João Requicha

Abstract

Distraction osteogenesis is a surgical technique widely used in orthopedic surgery for treatment of various pathological skeletal conditions, namely correction of limb-length discrepancies, angular deformity and treatment of distal and severely comminuted fractures, or bone defects through bone transport. The basic principle consists on the gradual distraction of two bone segments, previously submitted to a corticotomy and promptly fixated generally using of circular external skeletal fixation. New bone tissue is generated in the bone gap between the two segments. This review aims to describe the biological fundaments and principles of this technique, the surgical steps performed to attempt distraction osteogenesis, and its possible complications with main focus on its application in companion animals.

Keywords: distraction osteogenesis, principles, bone regeneration, companion animals

1. Introduction

Distraction osteogenesis (DO) can be defined as the mechanical induction of bone tissue produced after the section and slowly separation of two bone segments, stabilized and subjected through a slow, gradual, and stable distraction. This is possible due to the inherent capacity of bone tissue to regenerate and remodel according to the mechanical and tension forces to which it is gradually submitted [1, 2].

The DO is a technique widely used in human and veterinary medicine, both in adult and pediatric orthopedics. It is used in the treatment of various diseases such as limb length discrepancies, bone deformities secondary to trauma, infections or malformations, and even as a compensation after surgical excision of bone tumors [3]. The physiological bone growth is a result of the tension exercised over the bone physis and the soft tissue resistance. This forces act on the same plane but in opposite directions [4].

The basic of the procedure should respect the principles defined by Ilizarov, Bastiani, and other pioneers in orthopedic research: (i) the osteotomy will be of low energy preserving the vascularization and the soft tissue envelope; (ii) the fixation mechanism applied to both segments must be stable; (iii) after the corticotomy a

latency period will be applied, and (iv) the distraction rate (DR) must be appropriate for the level and type of bone in which osteogenesis is being performed [5].

After the separation of both segments, three temporal phases of DO can be defined: latency period, distraction period, and consolidation period [3].

2. Osteotomy and corticotomy

The DO procedure begins with the transverse section at a diaphyseal or metaphyseal level of the long bone to be elongated. Ilizarov described three methods to create fractures, including osteotomy, corticotomy, and osteoclasis. The osteogenic potential of the osteotomy or corticotomy depends on three main factors: the localization in bone, the type of technique used, and the latency period subsequently applied [6, 7].

Regarding the localization, some researchers in the past referred that the bone lengthening should be performed in the middle of the diaphysis of the long bone, and when necessary elongation was obtained, a bone graft from the ilium crest could be applied on the distraction focus to promote its consolidation. Later, Ilizarov recognized the metaphysis as the ideal site for the osteotomy, due to its massive trabecular bone area, rich in collateral vascularization, and higher potential for fracture recovery. Other researchers compared the regenerated bone quality at the diaphysis and metaphysis after DO, while using different latency periods. In the metaphysis, latency periods of 0 and 7 days allowed a greater osteogenesis and a faster remodeling and consolidation, when compared to the diaphysis elongation. A latency period of 14–21 days was associated with a premature consolidation in both regions. Bone mineralization of the newly formed tissue was faster at the metaphysis than at the diaphysis. Curiously, when there was no latency period, the distraction was successful and the consolidation faster. The latency of 7 days did not reveal the risk of premature consolidation; however, the consolidation and bone formation were slower than where there was no latency period. *Post mortem* torsion and bending test revealed that the bone tissue elongated on the metaphysis was tougher and more resistant. Histologically, the osteogenesis is observed to be based on intra-membranous ossification and, when a longer latency period is performed, increased proliferation of cartilaginous tissue at the osteotomy focus is detected, resulting in an endochondral ossification which may end up resulting in a slower process. The same study revealed that the metaphysis has more viable characteristics for the DO than the diaphysis [8].

Kojimoto and collaborators showed, in rabbits, the importance of the periosteum, referring that when it is removed, a bone callus is not formed and the bone lengthening can fail [9]. Ilizarov considered the preservation of the periosteum, and the medulla vascularization as mandatory to obtain better results on a DO [7, 10, 11]. Ilizarov developed the subperiostal osteotomy technique in which the anterior, medial, and lateral portions of the cortex are sectioned, and the posterior side is the manually fractured, thus preserving the medullar vasculature. Although Ilizarov defends the importance of the medullar vasculature, other authors question its importance [9, 12, 13].

3. Segment stabilization

The distraction is performed using an external fixation system, and this can be a circular Ilizarov or and longitudinal monoplane unilateral frame [3]. It is imperative to keep an adequate stabilization of the fracture, its alignment, and osteodistraction [11, 14].

The external fixator frame rigidity must prevent unnecessary micro-movements at the osteotomy site, but, at the same time, it should be compliant to allow bone

tissue inducting micro-movements along the axial axis [14–16]. A stable external fixator with less stiffness decreases the time to achieve bone consolidation. Moreover, the time of consolidation with low mechanical score (less rigid) is smaller when compared to more rigid fixations [2].

Kusec and colleagues compared the bone tissue formed by DO using a unilateral distractor and an Ilizarov distractor, in a population of 15 German Shepherd dogs. No histological or radiographic differences were found on the newly formed bone tissue. The regeneration progressed in centripetally from the cortex and the intramembranous ossification was predominant at the medullar portion of the distraction focus [17]. The Ilizarov fixator, comparing to Wagner, Orthofix, and Oxford unilateral frames, is also flexible with a consistent stiffness to bending moments in anteroposterior and lateral planes. Moreover, the Ilizarov fixator is more resistant to axial compression with increasing load and is more flexible in the axial direction compared with the other devices [18].

During bone lengthening, the distraction moment where the screws are tightened or loosened in the external device frame may create instability on the distraction focus and therefore adversely affect the procedure. The use of new compounds, such as highly dense plastics, interconnected with metal alloys, helps to prevent instability during the adjustment period [19].

4. Latency period

The latency period begins immediately after the osteotomy and extends to the beginning of the distraction. This may be characterized as a "rest" period after the corticotomy to allow a tissue response to the iatrogenic trauma. This response includes a proliferation of fibroblast and the induction of a state of periosteal reactivity, phenomena which occur at the beginning of a fracture regeneration [3]. The latency period allows an organization of the hematoma and the fibrous tissue matrix, which will serve as a mold to the osteoblast proliferation, that on the first 24 hours produce osteoid at the bone surfaces. This period also allows a periosteal and endosteal revascularization [7, 10, 20].

In rabbits, the importance of the latency period was demonstrated in a tibial DO. A 7-day latency period allowed a greater regeneration at the distraction focus and increased vasculature, in opposition to a DO without latency period characterized by a fibrous tissue formation [21]. Other studies showed that the existence of a latency period allows the formation of cartilaginous tissue which leads to regeneration based on an endochondral ossification, a mechanism that is slower that its intramembranous counterpart [8].

Regarding the duration of this period, there is no consensus and several studies report variable periods from 0 to 21 days [1, 7, 8, 10]. There are several factors that influence the appropriate latency period, such as: age, the osteotomy localization, the soft tissue trauma or the existence of a primary pathology. A longer latency period may allow a premature consolidation, being then necessary to produce another fracture in order to continue the lengthening. And a shorter latency period might predispose to a bone non-union [3]. In Veterinary Orthopedics, the recommended latency period is 2–3 days for immature animal or 5–7 days to mature animal [1], inferior to the usual 5–10 days reported in humans [3].

5. Distraction period

During the distraction period, the bone segments undergo a stable and constant tension force, becoming metabolically active. The formation of bone tissue occurs

along the distractive stress line, in the lengthening focus at the extremities of both bone segments. During this regenerative process, the bone tissue formation can reach 200–400 μm/day, which is 4–8 times superior to the physiological bone growth that occurs in the physis of a healthy growing dog [22].

With the distraction onset, tensile forces develop at the fracture focus, while at the same time collagen is deposited by proliferating fibroblast and organized into linear fibrils. This tissue becomes radiographically visible after 7–14 days of distraction, and with the continuous process, a radiolucency zone is formed at the center of the fracture focus, the fibrous interzone (FIZ). This zone divides the regenerated bone in equal parts, and it is rich in chondrocytes, fibroblast, and ovoid cell morphologically intermediate between a fibroblast and osteoblast. The FIZ remains avascular during most part of the distraction, after its completion, it is rapidly vascularized and mineralized during the consolidation period [3]. When the FIZ cells differentiate in osteoblasts, they begin to deposit bone matrix forming the micro-column formation zones (MCFZ). These micro-columns are similar to stalactites and stalagmites and are identified as cones of 150–200 μm. This mineralization proceeds longitudinally along the collagen fibers, parallel to the distraction forces. Between the FIZ and MCFZ, a connective tissue is formed, and this contains highly proliferative cells identical to those that arise in a primary ossification center [3].The fibroblast and osteoblast are arranged along the longitudinal collagen fibers at the distraction site and the later deposit osteoid directly into this fibrils [2] (**Figure 1**).

Although controversial, most histological studies regarding Ilizarov's method confirm that bone formation during a DO is primarily based in intramembranous ossification [8, 23]. In humans and in animal models of osteodistraction on both long bones and mandible, performed in dogs, rabbits, and sheep, intramembranous ossification prevails over its endochondral counterpart [9, 22, 24, 25], mainly on the ending stage [26]; however, three distinct ossification methods have already been identified. Endochondral ossification can be identified in all DO periods [9, 24, 27] and it is usually identified at the FIZ junctions and at new mineralized membranes originated from the corticotomy site [26, 28]. The ossification ratio between an intramembranous and endochondral ossification is 5–1, respectively [18, 26].

A third ossification phenomenon was histologically identified and termed transchondroid ossification, characterized by a bone formed from cells similar to chondrocytes and with a transition from fibrous tissue to chondroid bone tissue, a tissue intermediate between bone and cartilage, which undergoes a gradual transition to bone tissue without a blood capillary invasion [23, 28]. Other authors have

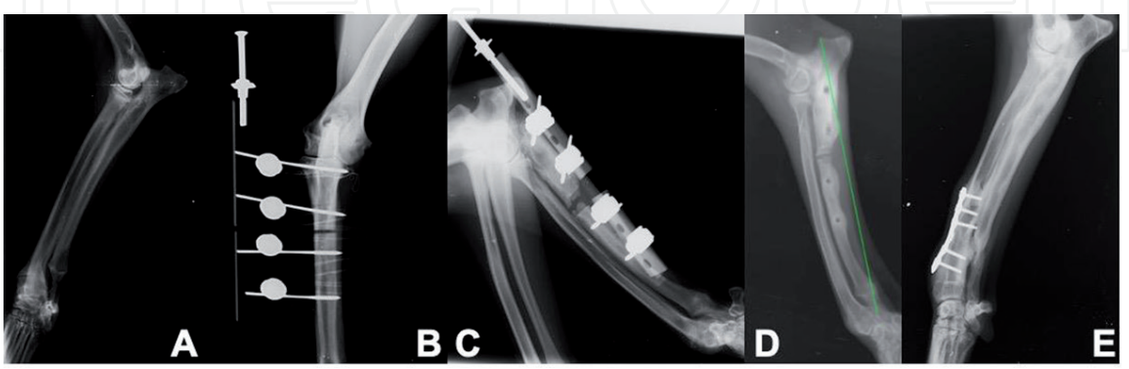

Figure 1.
Representative radiographic images of a distraction osteogenesis procedure performed in a 7-month-old female Greyhound dog due to a premature distal ulnar physis closure with proximal consequences in elbow joint. (A) Lateral view of the lower right thoracic limb. (B) Cranial view of the limb after the application of the distractor in the ulna. (C) Lateral view upon 11 days of distraction. (D) Lateral view at the end of the consolidation period and after the removal of the distractor. (E) After ulnar bone consolidation and lengthening, a realignment of the radius with an osteosynthesis plate was performed to fully rehabilitate the limb.

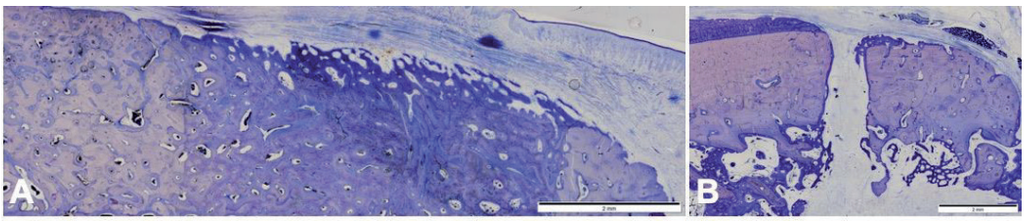

Figure 2.
Representative histologic images of a mandibular bone after distraction osteogenesis. (A) Distraction area successfully filled with new regenerated bone. (B) Bone defect occupied by connective tissue, a failure probably due to mobility of one of the fragments. Magnification ×40, Levai Laczko staining. Courtesy of Prof. Fernando Muñoz, Department of Clinical Veterinarian Sciences, University of Santiago de Compostela.

shown that cells similar to hypertrophied chondrocyte go through an osteogenic differentiation with deposition of type 1 and type 2 collagen fibers [29]. The cartilage that forms during a DO is usually located near the periosteum, but not within the limits of the cortex on the distraction focus [3] (**Figure 2**).

During the distraction period occurs an enormous angiogenic response. At the lengthening site, a peak of blood circulation nine times superior to that of normal bone tissue may occur. This hypervolemia persists for a significant amount of time, as it was shown that 17 weeks after the procedure the local volemia remains twice the normal value [23, 30].

It is believed that bone regeneration occurs in response to a slow and stable mechanical tensile force, applied to the bone callus and under which the living tissues become metabolically active, this phenomenon is called mechano-transduction [7, 10]. Ilizarov's experiments demonstrated that mitochondria of the skeletal muscular tissue hypertrophied and become more active, resulting in increased cellular volume and functional activity of the cell's nucleus [10].

During the distraction period, it is advised to do a radiographic assessment of the patient every 7–10 days, in order to evaluate the regenerated bone tissue, and if necessary, readjust the distraction rate (DR) [1]. Once the idealized bone length is achieved, the distraction ends. Marking the beginning of the consolidation period where the bone and osteoid are mineralized and remodeled [3].

6. Distraction rate and distraction rhythm

The distraction rate (DR), defined as the tension gradually applied to the bone, is measured in millimeters per day, the normal being 1 mm/day. However, this may vary according with the bone or the site of the bone we want to lengthen [3].

The total amount of distraction performed daily, the DR, is based on the same factors that should be considered for the ideal latency period [7, 10]. The typical DR in Veterinary Medicine should range from 0.75 to 2 mm/day, which is similar to what happens in Human Orthopedics [31–33]. Variables like age, osteotomy technique, and localization will influence the choice of a correct DR. We can correlate excessive DRs with muscular contractures and articular subluxations [34, 35]. The choice of an appropriate DR is essential in the prevention of premature consolidation of the regenerated tissue and soft tissue damage, as well as in the maintenance of articular congruity and biomechanical stability [1].

Ilizarov proposed an ideal DR of 1 mm/day for bone regeneration, and he based himself on his study in 120 dogs, using DR of 0.5, 1, and 2 mm/day. When using 0.5 mm/day, he noticed an increase in premature closures. And while using a DR of 2 mm/day Ilizarov reported increased tissue damage due to exceeding the tissues' revascularization capacity [14]. Recent studies suggest that DR between 0.5 and 2 mm/day

are appropriate, and that the ideal DR must be based on individual characteristics such as age, osteotomy site, and need for angular correction [12, 35].

The distraction rhythm (DRy), the number of lengthening times made per day, influences the quality and quantity of the regenerated bone tissue and is important in the preservation of the soft tissue integrity during the procedure [7, 10, 34]. Ilizarov observed, using a canine model, that by using an automatic distractor capable of performing a DRy of 60 times per day, would produce a significantly better quality of bone when compared with DRy of 1–4 times per day. A DR of 1 mm a day with a DRy of 4 times a day was determined as ideal [7, 10]. In a goat model of tibia lengthening, DRy of 1, 4, and 720 times per day would not affect the strength, rigidity, and histomorphometric characteristic of the regenerated bone and would not affect the somatosensory potential of the peripheral nerves [34, 36]. Another study using the same animal model concluded that increasing the DRy would result in less muscular degeneration [39]. In Veterinary Medicine, it is recommended DRy of 2–4 times per day [9, 18, 31, 33].

7. Consolidation period

When finished the distraction period, the external fixator is maintained in order to confer stability to the regenerated tissue and allow its mineralization and consolidation [3]. In this period, the FIZ starts to mineralize and the central region becomes radiographically sclerotic. During the following weeks, the columns of regenerated tissue become homogeneous as the primary bone tissue is replaced by Haversian bone. In small animals, it will take around 8–12 weeks to form a new cortex and medullary cavity [7, 10, 36, 37].

Over time, the longitudinally oriented trabeculae are transformed into transverse plaques, incorporating the collagen template [7, 8, 10, 36]. The bone microcolumns are covered with osteoblasts that actively produce osteoid. Each column is accompanied by a large vascular channel that preserves the ideal distance in order to allow a diffusion gradient between cells. The activity of bone cells during a DO is similar to what occurs during a fracture healing [8, 28, 38]. However, what happens at a tissue level, the continuous recruitment and activation of cells capable of producing and reabsorbing bone, significantly exceeds a fracture healing process [39]. Simultaneously during the extensive bone production, a remodeling occurs, producing *porosis* of the bone cortex and margins of the regenerated bone. After 2–3 months in animal and 4–6 months in humans, the Havers channels, through which blood vessels and nerves pass, are formed [11, 12, 38]. The bone marrow components, in the regenerated bone appear after 4 months. Bone remodeling is complete after 5–7 months in small animals and 12–24 months in humans. After this remodeling period, the mechanical integrity of the cortex is restored [1].

The consolidation period after a DO was investigated in a 20-year retrospective study, based on 115 animals submitted to a corticotomy and application of a circular external fixator [2]. The authors concluded that the radius requires less time to consolidate than the tibia and presented the hypothesis that this occurs due to during the march, the radius bears weight in a parallel axis and the tibia carries the weight through an oblique axis [40]. Another hypothesis is based on the fact that dogs bear around 60% of their weight on the thoracic limbs, therefore the weight carried by a radius is superior to what is supported by a tibia [41–43]. In experimental rabbit model, the effects of an angular osteotomy after a DO were studied, revealing that a 30° axis deviation at the distraction focus resulted in a 50% reduction of the regenerated bone [44]. In humans, the femur is referred to consolidate faster than the tibia [45]. Ilizarov's original technique described that the consolidation period before fixator removal should be 1 month/cm of new regenerated bone [46].

The bone formation can be controlled through tomography, scintigraphy, ultrasound, and bone densitometry; however, radiographs continue to be the more practical method to determine the consolidation efficiency and when the bone is ready to remove the external fixation system [1, 38].

Nowadays, numerous studies are focused on the molecular mechanism behind a DO, such as, the genetic expression of the bone morphogenic proteins (BMPs 2 and 4) which is induced by tension and mechanic stress [47, 48]. Other molecular signs, such as the insulin-like growth factor type 1 (IGF-1), transforming growth factor beta (TGFb) and fibroblastic growth factor 1 (FGF-1), associated with osteoblast proliferation and its differentiation from mesenchymal cells were identified at the distraction site [49, 50]. Another study identified that it is possible to accelerate the ossification process during a DO by administrating a recombinant homologous growth hormone [51].

Tissue engineering approaches have already been applied to promote bone regeneration at DO. The use of mesenchymal stem cells (MSCs) from autologous origin, isolated from the bone marrow or adipose tissue, or from human xenogeneic origin has been described in different animal models of DO like rats, rabbits, pigs, dogs, and sheep with promising outcomes; nonetheless many of the mechanism behind the process remain to be investigated, for example, the recruitment and activation of MSCs upon the initial stimulation by surgical trauma. Growth and differentiation factors, hormonal proteins, and pharmacological agents can be added in combination to the distraction site. The number of cells transplanted is measured in cell over DR (number of cells in millions divided by total distractions in millimeters) ranged from 0.03 to 5.00 M/mm. The cells can be injected after the distraction period, loaded into scaffolds and then transplanted to the distraction focus during the osteotomy or during the latency period [52]. Genetically modified MSCs have also been evaluated using growth and differentiation factors including bone morphogenetic protein-7 (BMP-7) [53, 54], BMP-2 [55, 56], basic fibroblast growth factor (bFGF) [57], transforming growth factor-β (TGFβ), and insulin-like growth factor-1 [58], as well as genes encoding transcription factors, such as osterix (Osx) [59, 60] and runt-related transcription factor 2 (Run×2) [61] with distinct effects reported in the improvement of bone regeneration [52].

8. Craniofacial distraction osteogenesis

Djasim and collaborators created guidelines for craniofacial DO. They collected data from dog, rat, sheep, goat, rabbit, pig, and rhesus monkey models based on data from previous craniofacial DO studies. With the premise that intramembranous bones of the skull have a different vascular supply compared to long bones, therefore DO parameters suitable for orthopedic DO might be suboptimal for craniofacial DO. They concluded that a latency period may not be necessary in some animals such as sheep and pigs, and in others it produces far better-quality bone tissue as seen in rats and rabbits. They reaffirmed that the ideal distraction rate should be 1 mm/day, which should be halved when using rats and determined an ideal consolidation period of 6–8 weeks [62]. Another review in mandibular DO showed that the latency period ranged from 2 to 7 days. The distraction rate ranged from 0.4 to 2.4 mm/day. The total distraction gap obtained ranged from 3.2 to 20 mm, and the consolidation period ranged from 4 days to 10 weeks [52].

9. Distraction osteogenesis after oncologic surgery

DO can also provide an option for limb sparing surgery upon resection of primary bone tumors, such as osteosarcomas. The bone transport osteogenesis (BTO),

an adaption of the DO technique, is used to preserve limb function after resection of large segmental bone defects. Briefly, after the tumor excision, an osteotomy is performed on the proximal bone segment, creating a distraction focus and resulting on a small portion of healthy bone which will act as the transport segment. Then using an external ring fixator, this segment is slowly distracted in the defect direction, creating regenerated tissue resulting in bone union and a bridged effect. The distraction should continue until 3 days after the segments touch in order to compress the distal healthy bone, turning it metabolically active, this process is called docking. Successful docking is achieved when the transport segment heals with the adjacent bone. It is possible to predict the timing of docking by measuring the distance between the two bones on radiographs and calculating the number of days required to achieve contact based upon the DR. The surgeon should consider grafting when the transport segment is approximately less than 0.5 cm from contact with the docking site. When owners strongly wish to avoid further surgery, autologous bone marrow graft, obtained from the patient, could be mixed with canine demineralized bone matrix (DBM) into the docking site, acting as a vehicle of mesenchymal stem cells and osteoinductive signals [63, 64].

BTO surged as an alternative to cadaveric allograft bone transports, which was seen as the main limb salvage procedure in alternative to amputation; however, complications such as non-union, graft fracture, and infection are referred in the literature. One study reported that nearly one half of the patients develop infection may be associated with the lack of intrinsic blood supply surrounding the allograft and tumor resection area [65]. This high complication rate could lead to soft tissue lost, chronic pain, non-weight-bearing lameness, multiple surgeries, and even amputation [66–68].

The extent of the needed tissue resection can be planned based on detailed radiographs, scintigraphy, or ideally, a preoperative magnetic resonance imaging (MRI) which will be essential to help build the fixator frame, and assess the extent of the tumor involvement within the bone marrow, as it commonly exceeds the extent detected on radiographs. The surgeon should plan to excise at least 2 cm of bone proximal to the most proximal extent of tumor identified [63]. The patients with better outcome in DO upon oncologic surgery are those whose tumors are located in the distal radius or ulna, due to bigger pancarpal arthrodesis success [64]. The best candidates for limb salvage are those whose tumors involve less than 50% of the bone and have minimal soft tissue involvement. In theory, the extension of tumor treatable with this technique is limited to by the ability to achieve appropriate margins. There must be at least enough bone remaining in the proximal radius to create a transport segment and to place three wires above the transport segment. Dogs with infected allografts after prior limb salvage surgery are suitable candidates for bone transport, unless they have had recent radiation therapy. Patients with pathologic fracture, multicentric neoplasia, metastasis or severe intercurrent health conditions should not be considered as favorable candidates [63].

After the tumor resection, BTO is similar to a conventional DO, a latency period of 3 days is sufficient unless the dog is receiving chemotherapy treatment. In those cases, a longer latency period of up to 7 days should be applied. Afterwards, the distraction should consist on a DR of 1 mm/day and DRy of 2–4 times a day. Immediately after a chemotherapy session, distraction should be ceased for 3 days before being restarted. This waiting period can be eliminated if the patient shows signs of premature consolidation. Radiographic reassessment should be made every 10–14 days during bone transport and every 3–4 weeks after docking. Some animals may require higher DR to prevent premature consolidation, while other may require occasional "resting" period of 2–5 days. If the regenerated bone begins to be progressively thinning, ductile, and with "hourglass" shape in radiographs, it is

recommended to slow or stop distraction for a few days. Conversely, if the wires in the transport segment begin to bend in the direction of distraction, the DR should increase for 2–3 days (1.5–2 mm/day) to help preventing premature consolidation. The radiographs and fixator should also be regularly evaluated to adjust DR and DRY, document broken wires, evidence of tumor recurrence, progression of mineralization of regenerate bone, and time of docking [63].

Fixators should be removed when peripheral bridging of the central radiolucent zone within the regenerate tissue is evident on radiographs, the columns of new bone are mineralized, and when the docking site union has been achieved. It can be difficult to evaluate the stability of the docking site before removing the fixator frame, due to the concentration of metal hardware. If doubt exists regarding effective union, the fixator removal can be delayed provided the patient is not having substantial soft-tissue problems. Osteosarcoma patients should be restaged every 2–3 months to evaluate for metastasis or local tumor recurrence [63].

Negative effects of systemic chemotherapy and radiotherapy are reported in distraction osteogenesis [69–71]. Chemotherapy likely impedes the osteoblasts to cope with the increased functional demand and compromises bone callus formation during a DO. High dose chemotherapy reduces colony forming unit fibroblast by 50% in the bone marrow, by 10% on cortical bone, and 20% in trabecular bone [72]. However, two studies compared patients who underwent DO with and without chemotherapy and it did not demonstrate any difference in the bone healing process between patient groups [73, 74]. The hypothesis proposed is that DO's effect on osteoblast may counteract the inhibitory effects of chemotherapy [75].

In humans, some bone sarcomas, most commonly Ewing sarcoma, adjuvant radiotherapy is a treatment option, being reported adverse effects of radiation therapy on up to 74% of patients [76–78], namely wound healing problems, infection, muscle and joint contracture, ankylosis, osteitis, non-union, pathological fractures, tendon adhesion, and radiation induced sarcoma [76–79]. In a rabbit tibia model, it was demonstrated that radiation exposure decreases the quantity and quality of regenerate and angiogenesis during a DO [80]. Also, in a rabbit mandible model, it was found that osteogenesis is delayed after a 60-Gy dose of radiation, even though viable osteoblast and osteocytes may still be present [81]. It is therefore likely that distraction osteogenesis is negatively affected by radiation [75].

10. Complications of distraction osteogenesis

The complication associated with a DO include muscular contractures, subluxations, vascular and nerve lesions, premature or delayed consolidation, and even bone non-union. The placement of intramedullary pins near a nerve or large caliber blood vessel can lead to damage on those structures during the lengthening [1].

Neuromuscular lesions are rarely associated with lengthening phases unless they exceed 30% of the limb size [33, 82, 83]. Subluxations are associated with muscular contractures and can occur in substantially excessive lengthening. Premature consolidations can be prevented with an adequate DR and DRy. Delayed consolidations are multifactorial but are more commonly reported cases where an excessive DR was applied. Bone non-union is on its own associated to an infectious process. A strict radiographic protocol allows a control, assessment, and readjustment in order to avoid these complications [1].

One of the limitations of this technique is the long period necessary for the newly formed bone to mature, mineralize, and consolidate. The external fixators must be kept until the end of the consolidation period in order to confer the stability necessary to obtain better quality bone [3].

During a femoral lengthening, the muscles inserted therein are responsible for the majority of the complication that may occur. The quadriceps, glutes, and abductors can influence the lengthening progression, and the tension exercised on the soft tissues causes pain, reduces the articular mobility, and deforms the regenerated bone column. To achieve a successful lengthening, it is imperative that one understands this concept and adjust the surgical technique and patient management to minimize its impact [5].

Stogov and collaborators showed, in dogs, that a high frequency (120 DRy) of 3 mm/day does not only produce viable bone, but also produce compensatory alterations to the muscle tissue that would prevent catabolic alterations on the anterior tibial muscle during a tibia elongation. These authors referred that a high frequency lengthening amount that does not exceed 15% of the initial tibial length, does not result in considerable damage to the anterior tibial muscle. Using a DR of 3 mm/day while increasing the DRy (180 automated distractions per day) can produce a consistent regenerated bone [84].

As mentioned before, the soft tissues are a limitation factor for the procedure [34, 82, 85]. Lengthening exceeding 20% the original bone measure is reported to damage peripheral nerves, muscular, and tendon structures. Thus, physical rehabilitation during the procedures could decrease the severity of the muscular contractures and prevents articular diseases. The double-level or bi-level lengthening, which consist on creating two fracture focus and therefore two focus of bone distraction can reduce by half the distraction period duration, dispersing the distraction forces applied at the soft tissues and reducing the degenerative effects [1]. The correction of biapical radial deformities in dogs has been described with success using bi-level hinged external fixators as posterior distraction [86].

Taking into consideration that the DO can also occur along a transverse axis, perpendicular to the longitudinal bone axis, it is also possible to perform a widening of bone tissue. Some authors have already successfully preformed bone transports, in order to correct a defect on a long bone they perform a DO on the contralateral bone and use the regenerated tissue as graft to the affected limb. It has been performed in the same bone tibia-tibia but also in ipsilateral ulnar and radial bone transports, tibial-humeral and fibular-tibial, and this procedure is also performed in human medicine [87].

It is worth referring a recent study in humans, which applied a multidirectional DO device, a new technique with the goal of correcting cranial deformities in children [88].

Conflict of interest

The authors declare no conflict of interest with any financial organization regarding the material discussed in the chapter.

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